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Revealing the cognitive contents of sleep to improve diagnosis and research

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Far from being an idle state, sleep plays restorative and transformative functions that are critical to both body and mind. As researchers and clinicians, we strive to evaluate sleep's effectiveness in completing these functions. However, this endeavor is challenged by the scarcity of function-specific biomarkers. Instead, we focus on the efficiency of sleep, using superficial measures such as total time asleep, number of arousals, or time spent at a specific sleep stage. In this letter, I will argue for the need to consider the cognitive content of sleep (i.e., the reactivated neurocognitive representations) in our clinical and scientific evaluation of sleep. Embracing recently developed methods for measuring and biasing the contents of sleep is a crucial step towards a deeper understanding of cognitive processing during sleep, paving the way toward improved diagnoses and treatments.

As a starting point, consider three employees, working together at an office under a meticulous manager. All three follow the same schedule – they arrive and leave at the same times, the number and durations of their breaks are comparable, and they spend similar amounts of time on their computers and filing documents (Figure 1a, top). Based on this information, their manager may assume that they are equally effective. However, only Employee A is truly hard-working and task oriented. Employee B works ineffectively and is easily distracted, whereas Employee C is engaged in active workspace sabotage. Just like superficial measures of workspace efficiency would prove futile in evaluating the employees' performance, so too do superficial measures of sleep efficiency fail to distinguish adaptive from maladaptive sleep (Figure 1a, bottom). Sleep effectiveness – like workspace effectiveness – must be judged in the context of function, incorporating sleep structure as well as substance.

The notion that sleep involves latent cognitive content – and that its content is linked with the function of sleep – rests on two pillars. The first line of evidence builds on dream reports. Although the history of attributing meaning to dreams goes back millennia, Freud's "The Interpretation of Dreams" is perhaps the most notable attempt at decoding sleep-related contents to improve well-being [1]. Freud didn't associate dream content with the function of sleep but rather speculated that dreams protect sleep against the workings of the inner psyche. More recent (and scientifically falsifiable) theories posit that dream contents play a role in the function of sleep (e.g., supporting memory consolidation and creativity [2]). However, dream reports are generally an inaccessible and unreliable method for monitoring the cognitive contents of sleep. Reports can only be collected upon awakening and are limited to conscious recollection, whereas some underlying cognitive processes may not require consciousness.

The second line of evidence suggesting that cognitive contents play a role in the function of sleep comes from the literature on memory consolidation. Overwhelming evidence from humans and nonhuman animals implicates sleep in the reactivation of memories, thereby strengthening them [3]. Unlike dreams, revealing the cognitive contents of memory reactivation does not rely on self-report or require awakenings. Whereas early work in nonhuman animals monitored reactivation on the cellular level (e.g., [4]), recent technological and methodological advancements in human cognitive neuroscience have allowed researchers to monitor memory reactivation noninvasively and in real time.

By leveraging neuroimaging techniques such as electroencephalography, magnetoencephalography, electrocorticography (EEG), and functional magnetic resonance imaging, together with computational approaches such as multivariate pattern analysis, the neural correlates of memory processing during sleep can be deciphered to reveal patterns of activity linked with the representations of memories. In general, two approaches can be used to unravel these representations (Figure 1b). First, patterns of brain activity could be identified during wake and then used as a template for interpreting the activity during sleep. For example, patients suffering from major depressive disorders could be exposed to stimuli linked with positive and negative affects during wake, establishing the patterns of EEG activity linked with these two types of stimuli. Then, the activity observed during sleep may be classified as one or the other, potentially providing a biomarker for maladaptive processing during sleep (Figure 1b, left). Neural patterns identified during wake have been successfully used to identify content reactivation during sleep in a few recent studies, demonstrating the potential of this method (e.g., [5–8]).

The second approach to unraveling content during sleep does not rely on data collected during wake. Instead, it considers the data collected during sleep and uses the similarities (or lack thereof) between different observed patterns as its dependent variable. For example, patients suffering from major depressive disorders may be exposed to negative, positive, and neutral words during sleep (Figure 1b, right). The activity observed following the neutral words will be correlated to that following the negative and positive words to determine whether the patients' information processing during sleep in negatively biased. Methods for monitoring cognitive processing during sleep based exclusively on sleep data have been successfully used in a number of recent studies (e.g., [9–12]).

To date, most studies monitoring and decoding the cognitive contents of sleep have been limited to memory reactivation in healthy participants. However, these methods' potential extends far beyond these realms. Sleep-related abnormalities are common in most psychiatric and neurological disorders, including major depressive disorder, post-traumatic stress disorder, and Alzheimer’s disease. Different hypotheses may drive studies that focus on specific sleep stages and classes of reactivated content in both healthy and clinical populations.

Some variations of the methods used to monitor content reactivation focus on time-locked responses to specific events occurring during sleep. For example, studies using targeted memory reactivation, the unobtrusive presentation of stimuli during sleep to bias memory consolidation [13], have analyzed neural activity time-locked to the onset of stimuli presented during sleep (e.g., [6,10,12]). However, other studies have focused on undisturbed sleep by focusing on spontaneous sleep-specific events, such as slow wave-spindle complexes (e.g., Figure 1b, left) [5], or even avoided relying on time-locked responses altogether [9].

Whereas most research has used content-specific methods to study memory reactivation, it is within reason to assume that actions, emotions, and intentions are also represented and reactivated within the sleeping brain. Unraveling the involvement of these higher-order cognitive constructs in sleep processing is the logical next step in evaluating sleep’s contribution to psychiatric and neurological disorders [3]. Combining novel methods to reveal sleep contents with manipulations to bias reactivation during sleep, such as targeted memory reactivation, may open new paths for discovery and treatment. Incorporating these methods in the lab and clinic holds the promise to revolutionize the way we evaluate sleep’s contribution to health, and specifically mental health.

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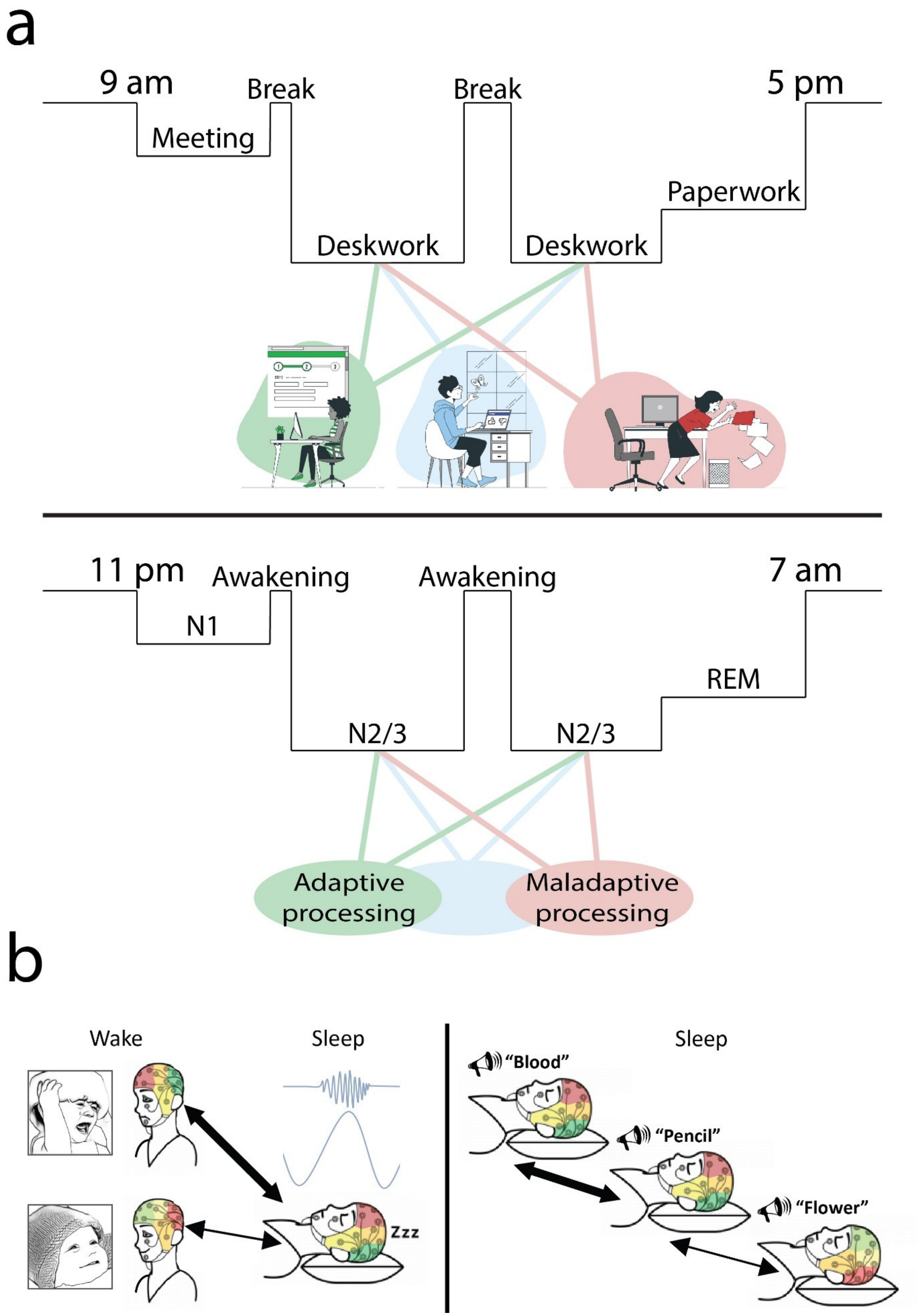
Figure 1: The cognitive contents of sleep as a novel dimension for evaluating sleep function. (a) A manager tasked with evaluating three employees would be hard-pressed to do so based only on superficial features such as hours of attendance and timing of breaks (top). In this example, whereas one employee is hard working (green), the others are unfocused (blue) or subversive (red). Similarly, judging the function of sleep based on sleep efficiency alone is impossible (bottom). The cognitive contents of sleep could prove useful in evaluating sleep for research and diagnosis. Illustrations by Storyset (free for use with attribution; https://storyset.com/business). (b) Different approaches for revealing sleep contents. Left – correlating wake-related patterns of brain activity to patterns of reactivation during slow-wave-spindle complexes. In this example, the patient's neural responses during sleep are correlated with wake-related responses to images linked with negative emotions (upper image) rather than positive emotions. Right – considering the correlation structure within patterns of sleep-related brain activity as a biomarker for adaptive vs maladaptive content processing. In this example, the patient's neural responses to neutral words (e.g., "pencil") are more similar to those evoked by negative words (e.g., "blood") relative to positive ones (e.g., "flower") , suggesting a negative bias in processing during sleep. In both examples, thicker arrows signify stronger correlations.



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"Flower"